

CLAIMS

1. A method of protecting a human subject from kidney
5 damage which comprises administering to the subject a
protective amount of an agent which is

(1) a polypeptide which is substantially structurally
identical or conservatively identical in sequence to a
10 reference protein selected from the group consisting of

(androgen related protein) NP_034724 and P15267;

(SON protein) NP_064357, AAF23121, NP_003094, and AAK07692;

15 (FUSE binding protein 1) NP_476513, NP_003893, and AAA17976;

(claudin 10) BAB32005, NP_067361, NP_076367, XP_127876,
NP_008915, and BAB710301;

20 (heat shock protein) BAA11035 and XP_036357;

(phosphotriesterase related protein) NP_032987 and
NP_109589;

25 (ubiquitin protein ligase Nedd-4) AAB63360, P46934, and
BAA07655; and

(Ac39/physophilin) NP_0385 and XP_08836;

30 or

(2) an expression vector encoding the polypeptide of (1)
above and expressible in a human cell, under conditions
conducive to expression of the polypeptide of (1);

35 where said agent protects said subject from kidney damage.

2. A method of protecting a human subject from kidney damage which comprises administering to the subject a protective amount of an agent which is

5 (1) an antagonist of a polypeptide, occurring in said subject, which is substantially structurally identical or conservatively identical in sequence to a reference protein selected from the group consisting of

10 (disabled-2 p96) AAG44669, AAH03064, P98082, and AAF23161;

(palmitoylated serine/threonine kinase) AAD02811, BAA89662, NP_035624, NP_003682, and CAA06700;

15 (tumor differentially expressed 1 protein) AAH11295, AAH22901, NO_036162, AAD54420, AAD22448, AAB48858, AAD54420, NP_006802, AAB48858, and AAD34641;

(cytochrome oxidase III) CAA24090, AAK17824, and AAL54598;

20 (TLH39 protein precursor) BAB22924, AAH22800, NP_114425, and AAG335730;

25 (hydroxysteroid dehydrogenase 4 delta <5>-3 beta) NP_032320, NP_000853, and AAA51831; and

(glutathione peroxidase III) BAB21943, BAB23686, and XP_087620; or

30 (2) an anti-sense vector which inhibits expression of said polypeptide in said subject,

where said agent protects said subject from kidney damage mediated by said polypeptide.

35

3. A method of protecting a human subject from kidney damage which comprises administering to the subject a protective amount of an agent which

5 (1)

5 (a) down-regulates expression of an "unfavorable" protein which is identifiable as a homologue in said subject of a mouse marker gene which is

10 (i) up-regulated in a first group of mice, which are experiencing or are prone to kidney damage, and/or

10 (ii) down-regulated in a second group of mice, which are protected against or otherwise less prone to kidney damage, relative to the other group, or

15 (b) is an antagonist for the expression product of the "unfavorable" gene, or

(c) degrades that product,

or

20

(2)

25 (a) up-regulates expression of a "favorable" protein which is identifiable as a homologue in said subject of a mouse marker gene which is

25 (i) down-regulated in said first group of mice and/or

30 (ii) up-regulated in said second group of mice, relative to the other group or

30

(b) is an agonist for the favorable protein, or

35 (c) inhibits the degradation of the favorable protein, or

35

(d) is said favorable protein or a protein which is substantially or conservatively identical thereto, or

(e) is an expression vector comprising a DNA sequence encoding said protein (d) and operably linked to a promoter whereby said protein (d) is expressed in cells of said subject which are transformed by said vector,
5 where said agent protects said subject from kidney damage.

4. A method of screening for human subjects who have developed, or are prone to development of, kidney damage, which comprises assaying tissue or body fluid samples from
10 said subjects to determine the level of expression of a "favorable" human marker gene, said human marker gene being substantially structurally identical or conservatively identical in sequence to a protein selected from the group consisting of

15 (androgen related protein) NP_034724 and P15267;

(SON protein) NP_064357, AAF23121, NP_003094, and AAK07692;

20 (FUSE binding protein 1) NP_476513, NP_003893, and AAA17976;

(claudin 10) BAB32005, NP_067361, NP_076367, XP_127876,
NP_008915, and BAB710301;

25 (heat shock protein) BAA11035 and XP_036357;

(phosphotriesterase related protein) NP_032987 and
NP_109589;

30 (ubiquitin protein ligase Nedd-4) AAB63360 , P46934, and
BAA07655; and

(Ac39/physophilin) NP_0385 and XP_08836;

35 and directly correlating the level of expression of said marker gene with the development of kidney damage in said patient.

5. A method of screening for human subjects who have developed, or are prone to development of, kidney damage, which comprises assaying tissue or body fluid samples from said subjects to determine the level of expression of an "unfavorable" human marker gene, said human marker gene being substantially structurally identical or conservatively identical in sequence to a protein selected from the group consisting of

10 (disabled-2 p96) AAG44669, AAH03064, P98082, and AAF23161;

(palmitylated serine/threonine kinase) AAD02811, BAA89662, NP_035624, NP_003682, and CAA06700;

15 (tumor differentially expressed 1 protein) AAH11295, AAH22901, NO_036162, AAD54420, AAD22448, AAB48858, AAD54420, NP_006802, AAB48858, and AAD34641;

(cytochrome oxidase III) CAA24090, AAK17824, and AAL54598;

20 (TLH39 protein precursor) BAB22924, AAH22800, NP_114425, and AAG335730;

25 (hydroxysteroid dehydrogenase 4 delta <5>-3 beta) NP_032320, NP_000853, and AAA51831; and

(glutathione peroxidase III) BAB21943, BAB23686, and XP_087620;

30 and inversely correlating the level of expression of said marker gene with the development of kidney damage in said patient.

35 6. A method of screening for human subjects who have developed, or are prone to development of, kidney damage, which comprises

assaying tissue or body fluid samples from said subjects to determine the level of expression of at least one human marker protein, where said human marker protein is identifiable as a homologue of a mouse marker gene which is expressed at different levels in a first group of mice who are experiencing or are prone to kidney damage and in a second group of mice protected against or otherwise less prone to kidney damage, and

correlating said level of expression of said human marker gene with the development of kidney damage in said subject.

7. The method of claims 4 or 6 in which the marker gene is one whose expression is down-regulated in the first group of mice.

8. The method of claims 4 or 6 in which the marker gene is one whose expression is up-regulated in the second group of mice and/or down-regulated in the first group of mice.

9. The method of claims 4 or 6 in which the first group of mice are treated with streptozotocin.

10. The method of claim 9 in which the second group of mice are treated with streptozotocin, but are genetically modified mice protected from diabetes-induced kidney damage by virtue of their genetic modification.

11. The method of claim 10 in which the genetically modified mice are transgenic mice which express a growth hormone (GH) mutant which is a GH receptor antagonist which antagonizes a growth hormone endogenously expressed by said mice.

12. The method of claim 10 in which the genetically modified mice are mice which do not express a functional growth hormone receptor binding protein (GHRBP).

13. The method of claim 9 in which the second group of mice are nontransgenic mice which are not treated with streptozotocin.

14. The method of any one of claims 4-6 in which the level of expression of the marker protein is ascertained by measuring the level of the corresponding messenger RNA.

15. The method of any one of claims 4-6 in which the level of expression is ascertained by measuring the level of a protein encoded by said marker gene.

5 16. The method of any one of claims 1-8, 14-15 in which the subjects are diabetic and the kidney damage is, at least in part, diabetes-induced.

17. The method of any one of claims 1-8, 14,15 in which the subjects are hyperinsulinemic.

10 18. The method of claims 4 or 6 in which the first group of mice exhibit kidney damage.

19. The method of claims 4 or 6 in which the first group of mice are genetically modified to overproduce growth hormone.

15 20. The method of claim 18 in which the first group of mice produce a heterologous growth hormone in addition to mouse growth hormone.

22. The method of claim 18 in which the second group of mice are normal mice.

20 23. The method of any one of claims 1-3 in which the agent is a DNA, or is encodable by a DNA, which specifically hybridizes to the recited DNA strand of any of SEQ ID NOS: 1-34, or to the complementary strand thereof.

25 24. The method of any one of claims 1, 2, 4 or 5 in which said polypeptide is at least 80% identical or at least highly conservatively identical to said reference protein.

25 25. The method of any one of claims 1, 2, 4 , 5 or 24 in which said polypeptide is at least 90% identical to said reference protein.

30 26. The method of any one of claims 1, 2, 4 or 5 in which said polypeptide is identical to said reference protein.

35 27. The method of claims 4 or 6 in which said homologue is identifiable by a BLASTN or BLASTX search conducted, using any of SEQ ID NOS:1-34 as a query sequence, on the NCBI Entrez sequence database(s), on or before the filing date of the instant application, and the E value calculated by BLASTX or BLASTN for the alignment of that homologue, or

cDNA encoding that homologue, to the query sequence is less than e-10.

28. The method of claim 27 in which the E value calculated by BLASTN or BLASTX would be less than e-15, more 5 preferably less than e-20, still more preferably less than e-40, even more preferably less than e-60, considerably more preferably less than e-80, and most preferably less than e-100.